Sleep in Childhood and Adolescence: Age specific sleep characteristics, common sleep disturbances and associated difficulties

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Abstract

Sleep changes throughout the lifespan, with particularly salient alterations occurring during the first few years of life, as well as during the transition from childhood to adolescence. Such changes are partly the result of brain maturation; complex changes in the organisation of the circadian system; as well as changes in daily routine, environmental demands and responsibilities. Despite the automaticity of sleep, given that it is governed by a host of complex mechanisms, there are times when sleep becomes disturbed. Sleep disturbances in childhood are common and may stem from behavioural difficulties or abnormalities in physiological processes – and, in some cases manifest into diagnosable sleep disorders. As well as occurring exclusively, childhood sleep disturbances often co-occur with other difficulties. The purpose of this chapter is to outline the neurobiology of typical sleep/wake processes, and describe changes in sleep physiology and architecture from birth to adulthood. Furthermore, common childhood sleep disorders are described as are their associations with other traits, including all of the syndromes presented in this handbook: ASDs, ADHD, schizophrenia, and emotional/ behavioural difficulties. Throughout, we attempt to explain possible mechanisms underlying these disorders and their associations.

Keywords: Adolescent, Child, Circadian, Emotion, Psychopathology, Polysomnography, Sleep

Sleep changes throughout the lifespan, with particularly salient alterations occurring during the first few years of life, as well as during the transition from childhood to adolescence. Such changes are partly the result of the maturation of the brain during this developmental period; complex changes in the organisation of the circadian system; as well as changes in daily routine, environmental demands and responsibilities. Such changes may reflect the different functions of sleep at different time points. While there is on-going debate as to the functions of sleep, sleep has been suggested to serve a variety of functions including facilitating learning and memory processes and brain plasticity (Maquet 2001), synaptic homeostasis (Tononi and Cirelli 2006), restoration of the brain and body through the release of growth hormone during slow wave sleep (SWS) (Sassin et al. 1969), and energy conservation (Siegel 2009). While sleep is a largely automatic process, sleep disturbances[1] are common in childhood. These may range from common behavioural difficulties (e.g. bedtime resistance), to less common diagnosable sleep disorders (e.g. dyssomnias: abnormalities with the timing, duration or quality of sleep; and parasomnias: atypical behaviours occurring during the sleep period). Sleep disturbances during development are associated with a plethora of childhood difficulties, including autistic spectrum disorders (ASDs), attention deficit hyperactivity disorder (ADHD), emotional and behavioural difficulties. There are likely to be multiple reasons for these associations, including both genetic and environmental influences; as well as the hormonal, neurological and psychological processes stemming from these aetiological factors. One possible mechanism by which sleep may be associated with other difficulties is likely to be due to underlying neurobiological factors affecting both phenotypes. Sleep and circadian rhythms are influenced by a number of neurotransmitter systems, and many of these systems are also implicated in numerous psychiatric disorders (Wulff et al. 2010). Hence, it is no wonder that disruption of sleep is so often associated with other difficulties. Given the importance of sleep for growth and development, it is unsurprising that sleep disturbances are linked to other disorders.

The aims of this chapter are to provide an overview of 1) the neurobiology of normal sleep/wake processes; 2) sleep physiology and architecture occurring from birth to adulthood; 3) common childhood sleep disorders; and 4) current knowledge regarding the associations between sleep disturbances and associated traits (including all of the syndromes presented earlier in this handbook: ASDs, ADHD, schizophrenia, emotional and behavioural difficulties), and the possible mechanisms underlying these associations. Understanding more about the associations between sleep and associated difficulties throughout childhood and adolescence holds promise of informing

[1] We use the term 'sleep disturbances' throughout this chapter to encompass both behavioural 'difficulties' with sleep and 'sleep disorders'.

us further about neurobiology for sleep/ wakefulness and also for the difficulties with which sleep disturbances are associated.

Neurobiology of sleep and wake

According to the 'Two-process model' proposed by Borbély (1982), the sleep-wake cycle is controlled by the interaction between a homeostatic and a circadian process (Borbély 1982; Daan et al. 1984). The homeostatic process can be described as the accumulation of sleep pressure (i.e. the increase in sleepiness as wakefulness progresses), or 'Process S', which rises during the day reaching its peak at sleep onset, and decreases during sleep such that the homeostat is restored to baseline levels. To some extent, sleep pressure is a function of time spent awake and the duration of prior sleep. 'Process S' may be due to the accumulation of sleep-promoting substances (such as adenosine – a biochemical substance that inhibits neurons associated with arousal) during wakefulness, which then dissipates during sleep (Porkka-Heiskanen et al. 2002). Underlying the homeostatic process is a circadian process, which maintains 24-hour daily rhythms by a self-sustained oscillator located in the suprachiasmatic nuclei (SCN) of the hypothalamus. This 'circadian pacemaker' ensures entrainment of biological rhythms (such as the rhythms of core body temperature, cortisol and melatonin secretion) to external time-cues (such as light and temperature), thus influencing the timing of sleep, independent of the homeostatic process. These processes are considered to develop independently and it is likely that many genetic, neurobiological and environmental factors are involved (Gregory and Franken 2009).

The transition from wake to sleep is governed by opposing mechanisms controlling arousal. Arousal related wake-promoting mechanisms are thought to originate in the brainstem, hypothalamus and basal forebrain which promote arousal via the activity of neurochemical systems controlling the neurotransmitters acetylcholine (ACh), glutamate, gamma-aminobutyric acid (GABA), the monoamines (noradrenaline [NA], histamine [HA], serotonin [SA] and dopamine [DA]), and orexin/hypocretin. These neurotransmitters (with the exception of GABA) have excitatory effects on target neurons and also modulate the excitatory and inhibitory effects of other inputs on target neurons to promote cortical activation during wakefulness in response to sensory input (España and Scammell 2011). Largely speaking, the monoamines are most active during wakefulness, decrease during NREM sleep and are mostly absent during REM sleep (Aston-Jones and Bloom 1981; Saper et al. 2010). Orexin neurons, however, are mostly active during wakefulness and silent during both NREM and REM sleep (Mileykovskiy et al. 2005; Lee et al. 2005). Additionally, orexin has been proposed to be responsible for the stability of the sleep-wake switch, controlling the transition from wake to sleep in a timely manner, preventing unexpected and sudden lapses into sleep, such as those typical of the sleep disorder narcolepsy (a sleep disorder characterised by frequent,

unintentional lapses into sleep) (Saper et al. 2001). In contrast, GABA is an inhibitory neurotransmitter which inhibits the projections from the arousal systems, including aminergic and orexigenic nuclei, thus decreasing arousal, and is particularly active during NREM sleep (España and Scammell 2011).

Sleep physiology and architectural changes from birth to adulthood

Although sleep is largely idiosyncratic, there are commonalities in the changes in sleep that occur across the lifespan, both biologically (in terms of sleep physiology) and behaviourally (in terms of sleep patterns). The sleep of a newborn infant is markedly different from that of a child, teenager or adult, and the most dramatic changes in sleep occur in the first 2 years of life. One defining feature of the sleep of newborn infants is that they do not possess a stable sleep-wake cycle aligned to the 24 hour day-night cycle. This is largely due to the fact that circadian rhythms only begin to become synchronised to day-night cycles around 2-3 months after birth (Mistlberger and Rusak 2011) and become fully expressed around 6 months (Herman 2005). The circadian system in newborn infants generates non-24 hour rhythms. As infants typically require regular feeding at schedules throughout the day, 'ultradian' (<24 hours) cycles emerge, during which sleep may occur just as much during the day as during the night (Lockley and Foster 2012). Around 2-3 months sleep becomes more consolidated, with a major sleep period dominating the night with shorter naps during the day. A regular sleep-wake cycle becomes fully established by 2 years of age, with quantity and duration of naps gradually decreasing in early childhood (Adair and Bauchner 1993).

As early as from birth, sleep is characterised by cyclic alternations between non-rapid eye movement (NREM) (known as 'quiet' sleep in infancy) and rapid eye movement (REM) sleep (known as 'active' sleep in infancy) which differs to cyclic alternations occurring in adulthood in both structure and composition (Sheldon 2005b). In a typical night, adults cycle through lighter stages of NREM sleep (stages 1 and 2), entering deeper stages of slow wave sleep (stages 3 and 4, which together constitute slow wave sleep [SWS]) before entering REM sleep. Infants, however, typically enter REM sleep prior to NREM sleep (Jenni and Dahl 2008). This cyclic alternation between NREM-REM sleep typically takes approximately 90 minutes in adults; compared to approximately 50-60 minutes in infants (Carskadon and Dement 2011). Furthermore, sleep spindles (a sharp increase in oscillatory brain activity with a frequency of between 12-14Hz, characteristic of stage 2 NREM sleep) are absent in newborn infants, as are the deeper stages 3 and 4 of NREM sleep (SWS). By around 2-6 months of age, the brain is more fully developed in terms of structure and function, and the ability to support slow wave activity (SWA: brain activity in the delta frequency range, 0.5-4Hz) coincides with the emergence of NREM stages 3 and 4 (Carskadon and Dement 2011). The NREM-REM cycle

gradually increases from the 60 minutes observed in infancy, to 75 minutes by 2 years of age, and around 90 minutes by 6 years of age (the same as observed in adulthood) (Lockley and Foster 2012).

Beyond a year, the ordering of sleep stages in NREM-REM cycles in infants largely reflects that of adults' (Sheldon 2005b). However the relative proportions of sleep stages across the night vary considerably. Newborn infants spend around 17-19 hours of the day sleeping, with REM sleep occupying around 50-80% of total sleep, reducing to around a third by 6 months of age, and approximately a quarter around 2 years of age (Carskadon and Dement 2011; Empson 2002; Lockley and Foster 2012, and see Table 1). While little of the sleep period consists of stage 2 sleep in infancy, stage 2 sleep gradually increases during childhood at the expense of REM and SWS. The gradual decrease in REM sleep continues into adolescence (Dahl 1996). Whereas the function of different sleep stages is still debated, it is likely that the large proportion of REM sleep in infancy is necessary for the acquisition and consolidation of the vast amount of information that infants are presented with in this early stage of life (Lockley and Foster 2012). Furthermore, both NREM and REM sleep appear to be important for the maturation of the brain (Peirano and Algarin 2007), which makes it unsurprising that neonates spend the majority of their day sleeping. Brain activity resembling that of SWS begins to emerge in the first few months of life (Sheldon 2005b), and the proportion of SWS is greatest during childhood than in any other period in life, which reduces by approximately 40% during adolescence (Carskadon and Dement 2011), highlighting the potential importance of sleep on maturational processes and the growth of new connections. The infant sleep period of an average 17-19 hours per day gradually reduces to around 8-9 hours by adolescence (Iglowstein et al. 2003, and see Figure 1 for sleep stage changes across the lifespan).

Another dramatic change in sleeping patterns from childhood through to adolescence is the delay of the circadian rhythm (Crowley et al. 2007). Bedtimes and rise times begin to occur much later, and this shift towards 'eveningness' (i.e. a tendency to wake late in the morning and go to bed late at night) increases during adolescence to a phase delay of around 3 hours (i.e. a delay in the secretion of endogenous markers of circadian rhythmicity), with a peak (and thus the latest sleep time) at around the age of 22 years. This peak is thought to be a biological marker of the end of adolescence (Roenneberg et al. 2004). Rather than simply being a lengthening of the circadian period in adolescents, this phase delay is considered to be the result of a reorganisation of the circadian system and its interaction with homeostatic sleep pressure (Carskadon 2008; Hagenauer et al. 2009). Indeed, adolescents exhibit a slower build-up of, and less sensitivity to, homeostatic sleep pressure such that they can stay up later during the evening (Jenni et al. 2005). Coupled with their delayed phase, together these mechanisms are responsible for the delay in sleep times. The delay in

sleep times also correlates with pubertal development suggesting a role for hormones in the reorganisation of the circadian system (Hagenauer et al. 2009).

While a normal part of maturational development, the delay in the circadian rhythm, and by consequence later sleep times, can be detrimental to the health and well-being of adolescents. Societal demands (including early school start times and social commitments) are out-of-sync with the biological clock, requiring adolescents to rise at times not in accordance with their circadian rhythms. Indeed, school start times in at least some schools in the USA become progressively earlier with increasing school grade (Carskadon et al. 1998) – which is at odds with adolescents' biological sleep times. Early school start times have been shown to contribute to adolescent sleep deprivation, given that bedtimes are not routinely moved earlier despite the need to rise early, resulting in a progressively shorter sleep period and consequential daytime sleepiness (Carskadon et al. 1998). While adolescents tend to make up this loss of sleep by sleeping in during the weekends, such disruption of circadian rhythmicity and reduction of overall sleep length (imposed by early school start times) may be detrimental. Indeed, altered sleep patterns and sleep loss during adolescence have been associated with decrements in cognitive functioning, mood regulation and academic performance (Carskadon et al. 2004). Delaying school start times by as little as 30 minutes has been shown to have beneficial effects on alertness, mood, and general health (Owens et al. 2010). Although delaying school start times has not yet been widely implemented, maintaining good sleep hygiene practices (e.g. careful control of behavioural and environmental factors preceding sleep) may help synchronise the circadian system to societal demands. For example, careful control of lighting conditions immediately before bed, during the night-time and during the day may be important for maintaining regular sleep-wake patterns by synchronising the circadian clock (Herman 2005).

Neurobiological changes through childhood and adolescence

Anatomical changes in brain size and structure may underlie some of the changes that we see across development in terms of the timing and structure of sleep. Before adolescence the brain undergoes a surge of growth in both grey and white matter, with a peak before puberty coinciding with the pronunciation of SWA (Kurth et al. 2012; Kurth et al. 2010). Neuroimaging studies have demonstrated that between the ages of 4-20 years cortical white matter increases linearly, while cortical grey matter changes in a non-linear fashion, peaking in pre-adolescence and decreasing post-adolescence (Giedd et al. 1999; Pfefferbaum et al. 1994). The decrease in grey matter following puberty likely reflects the decline in synaptic density (through synaptic pruning) during this time (Huttenlocher and Dabholkar 1997; Huttenlocher 1979), thus highlighting that adolescence is an important period for cortical maturation. Brain energy consumption also follows a similar pattern

(Chugani et al. 1987). It is possible that the pre-adolescence increases in white and grey matter occur in response to the constant flow of incoming information from external stimuli – information that needs to be efficiently assimilated and stored. The post-adolescence decreases in grey matter, however, may be due to selective synaptic pruning of redundant connections and the decline in the extent of learning post-adolescence relative to the abundance of new memories formed during childhood. A reduction in the number of synapses is thought to give rise to dampened EEG amplitude characteristic of SWS (Tarokh and Carskadon 2010).

However, synaptic pruning and metabolic changes are paralleled by changes in sleep depth, as indexed by SWA, which increases linearly until puberty, after which it decreases during adolescence and into adulthood (Campbell and Feinberg 2009; Feinberg 1989; Buchmann et al. 2011). Thus, as a result of the net decrease of synaptic activity, SWA becomes lower in amplitude at a proportional rate. This association between synaptic density, energy metabolism and EEG activity during sleep suggests that SWA may be a marker for cortical maturation during adolescence. Indeed, Buchmann and colleagues (2011) demonstrated that sleep EEG, most notably in the SWA frequency range, was associated with grey matter volume/thickness particularly in brain regions undergoing maturation during adolescence (such as the medial parietal lobe and the prefrontal cortex). Others have demonstrated that the maturation of SWA precedes the thinning of grey matter (Kurth et al. 2012). Whether the correlation between SWA and grey matter density is purely coincident or whether these changes reflect active interactions is yet to be determined.

Sleep disturbances in children and adolescents

As evidenced above, normal sleep is a largely automatic process, governed by a host of complex processes. However, sleep disturbances are common in childhood, and may be due to a number of factors, including environmental and psychological processes; as well as genetic, hormonal, and neurobiological mechanisms. Sleep disturbances may range from behavioural difficulties (e.g. bedtime resistance), to diagnosable sleep disorders (e.g. sleepwalking). Despite the existence of well-defined diagnostic criteria for numerous primary sleep disorders e.g. the Diagnostic and Statistical Manual of Mental Disorders [DSM] (American Psychiatric Association 2000); and the International Classification of Sleep Disorders [ICSD] (American Academy of Sleep Medicine 2005, [AASM]), studies of sleep disturbances in childhood and adolesence have tended to focus on a more broad definition of 'sleep disturbances' rather than assessing specific diagnoses. This may be largely due to the numerous ways that sleep disturbances can be assessed (including subjective and objective measures), reported (parent vs. child report), and the diagnostic classification system used. Using a broad definition, sleep disturbances are thought to be prevalent in up to 40% of children and adolescents (Mindell and Meltzer 2008), and may impact a number of domains including cognitive,

emotional, behavioural and academic functioning (Jenni and Dahl 2008). Furthermore, one study found that sleep disturbances in childhood were associated with poorer neuropsychological functioning in adolescence (Gregory et al. 2009a). When considering specific diagnoses, a substantial number of sleep disorders common in children and adolescents have been identified (for example see the ICSD, AASM, 2005). A selection of sleep difficulties have been chosen for further discussion here, including poor sleep hygiene, delayed sleep phase syndrome (DSPS), nightmares, behavioural insomnia of childhood (BIC), psychophysiological or primary insomnia, parasomnias, sleep-related breathing disorders (SBD) including obstructive sleep apnea (OSA), narcolepsy, and restless legs syndrome (RLS).

Poor sleep hygiene and Delayed Sleep Phase Syndrome (DSPS): A survey in the USA of parent/caregiver reports of their children's sleep and behaviour demonstrated that around a third of pre-schoolers and young children actually obtain less sleep than their parents' consider to be enough (National Sleep Foundation 2004). Furthermore, around a quarter of pre-schoolers, and a third of younger and older school-aged children, habitually consumed caffeinated beverages on a daily basis. Pre-schoolers, younger and older children also commonly have electronic devices in their bedrooms (including televisions, phones, computers), the proportion of which increases with age. For instance, around a quarter of toddlers to around half of school-aged children have a TV in the bedroom (National Sleep Foundation 2004). Furthermore, around a half of adolescents are likely to use electronic devices within the hour immediately preceding sleep (National Sleep Foundation 2011). Unsurprisingly, these behaviours and practices have been found to reduce sleep duration and quality (National Sleep Foundation 2004). While being problematic by their own nature, poor sleep hygiene practices may also exacerbate other difficulties such as DSPS. DSPS is characterised by late sleep onset times and wake up times and presents as an extreme tendency towards eveningness which is out-of-sync with societal norms (AASM, 2005). In children and adolescents, it is possible that disruptions from sleep may be problematic not only for the sufferer, but for other family members whose sleep may be disrupted by the abnormalities of sleep from the primary complainant (Wiggs 2007). Thus it is possible that sleep patterns characteristic of children with DSPS may also be disruptive to parents given that the child's sleep times may be substantially later than desired by parents. Behavioural abnormalities in the timing of sleep are coupled with shifts in biological indices of the circadian rhythm such as phase delays of melatonin secretion and core body temperature (Chang et al. 2009). Using electronic devices that emit blue-wave length light (such as mobile phones, tablet computers, televisions) late at night may further reinforce the delay in the circadian rhythm, given the known phase shifting effects of light (Minors et al. 1991).

Behavioural insomnia of childhood: Difficulties associated with BIC (including bedtime resistance and frequent night-wakings) are perhaps the most prevalent sleep disturbance of childhood, affecting around 20-30% of children aged up to 3 years (Sadeh et al. 2009). As a clinical diagnosis, BIC can be categorised into three subtypes, including sleep onset association (SOA), limit setting and combined types (AASM, 2005). SOA is typically observed in infants and toddlers, and is the reliance on inappropriate associations in the sleeping environment required to get to sleep, such as a pacifier, rocking, watching TV or holding a particular object such as a bottle. Children with SOA typically have frequent night-wakings and have trouble getting back to sleep following such arousals. While arousals from sleep are a usual part of sleep architecture (Sadeh 1994), parents of children experiencing SOA consider their child's night-wakings to occur much more frequently, and attempts by the child to return to sleep independently are often unsuccessful without the aid of a comforting stimulus (Moore 2012). Often the presence of a parent is necessary for the child to return to sleep in cases where parents form a part of the sleep association (such as holding a bottle or feeding), and thus parental presence in the bedroom often predicts the likelihood of night-wakings in children (Sadeh et al. 2009). Limit setting disorder, most typically observed in middle childhood and early adolescence (Sheldon 2005a), is the stalling or refusal to go to bed, which stems from inadequate limits on bedtimes set by parents. Often the child's refusal to go to bed is reinforced when parents give in to the child and allow them to determine their own sleep time and bedtime routine (Moore 2012). Once limits are set, however, problems are typically eliminated. The combined type, involving both inappropriate sleep associations and difficulties with limit setting, often manifests as a refusal to go to bed accompanied by crying or tantrums, which results in the parent comforting the child in the bedroom - thus reinforcing the behaviour and creating negative sleep associations consistent with SOA (Moore 2012). Behavioural interventions, such as improved sleep hygiene, including a bedtime routine, and extinction (preventing reinforcement of inappropriate behaviour, allowing the child to break negative sleep associations) are effective treatments for BIC (Mindell et al. 2006).

In adulthood, insomnia is typically characterised by difficulties initiating and maintaining sleep, awakening too early, and/or feeling that the sleep period was nonrestorative or unrefreshing (AASM, 2005). These symptoms may be a psychophysiological manifestation resulting from cognitive arousal during the pre-sleep period focused on worrisome thoughts about the consequences of not being able to sleep. Psychophysiological insomnia may be more evident in older children and adolescents given the advancement in cognitive abilities leading them to be concerned and worried about the impact of their sleep on daytime behaviour. Indeed there is a growing body of evidence that catastrophic worry, dysfunctional beliefs about sleep and cognitive pre-sleep arousal are characteristic of children, teenagers and young adults reported to experience sleep disturbances

(Barclay and Gregory 2010; Gregory et al. 2009b; Gregory et al. 2010; Alfano et al. 2010; Gregory et al. 2008b; Alfano et al. 2009).

Parasomnias: Other sleep disorders seen in childhood and adolescence are primarily physiological in nature including some parasomnias, OSA, narcolepsy, and RLS. Parasomnias can be defined as atypical behaviours which occur during the sleep period, such as sleepwalking, sleeptalking, bruxism, nightmares, bad dreams, night terrors and enuresis, which may lead to intermittent awakening (AASM, 2005). While many of these sleep disorders may be considered to be a normal part of development, they become problematic when they are frequent and persist beyond certain ages (AASM, 2005).

Sleepwalking: Sleepwalking is prevalent in around 17% of children, and while it can occur in young children as soon as they have the ability to walk, it peaks around the age of 8-12 years (AASM, 2005). Sleepwalking is characterised by a series of complex behaviours often accompanied by impaired judgement and altered state of consciousness (AASM, 2005). Although sleepwalking often disappears following puberty, it may persist into adolescence and adulthood (approximately 4% of adults experience sleepwalking). Sleepwalking usually occurs during arousals from SWS, and given that the proportion of the night spent in SWS is maximal during childhood, it is no surprise that it is more prevalent in children (Carskadon and Dement 2011). During sleepwalking, the typical NREM-REM sleep cycle is usually preserved although SWS dysregulation, in the form of increased EEG activity in the delta range prior to an arousal, increased SWA across NREM stages and high SWA fragmentation, has been observed (AASM, 2005). Sleepwalking is influenced by a combination of predisposing and precipitating factors. Genetic factors have consistently been shown to exert a strong influence in its occurrence, demonstrated by twin studies (see Barclay and Gregory 2013, for a review). Precipitants have also been identified, including sleep deprivation (possibly due to the increased proportion of rebound SWS, that is, an increase in the proportion of sleep defined as SWS following sleep deprivation, Bonnet 2011), as well as conditions affecting the head such as head injury, migraines, encephalitis and stroke, and events associated with psychological distress, amongst others (AASM, 2005).

Sleeptalking: Sleeptalking is highly prevalent occurring in around 50% of young children (AASM, 2005), and can occur independently, or may be associated with a bout of sleepwalking or disorders such as REM sleep behaviour disorder (RBD), although may arise from any sleep stage. Like sleepwalking, twin studies have demonstrated that genetic factors contribute to around half the liability to sleeptalking (Hublin et al. 1998b).

Bruxism: Bruxism is a movement disorder characterised by teeth grinding or clenching during sleep, resulting from tonic or phasic muscle contractions, which can often lead to wearing of

teeth, tooth and muscle pain, headaches and arousals from sleep (AASM, 2005). Bruxism is mostly present in children, with prevalence rates ranging from 14-17%, which decreases to around 12% in adolescents and 8% in adults (AASM, 2005). Like other parasomnias, genetic factors appear to be important, accounting for ~40% of liability to bruxism (Hublin et al. 1998a), but episodes can also be triggered by precipitating factors such as anxiety and stressful life events (Ohayon et al. 2001).

Nightmares: Nightmares and bad dreams are common in childhood and at least 75% of children have experienced a nightmare at least once (Mindell and Barrett 2002). Yet nightmares are only considered problematic when they are accompanied by other disorders such as insomnia or anxiety (Moore 2012). Approximately 10-50% of children aged 3-5 years, experience nightmares that are severe enough to disturb parents (AASM, 2005). Nightmares (which usually occur in REM sleep) and bad dreams are often thought to be synonymous, yet the distinction between these terms is that nightmares result in the child awakening while bad dreams do not necessarily (AASM, 2005). In both cases, the child is able to remember the content of the nightmare or dream. On the contrary, following sleep terrors, which occur in around 3% of children and manifest as a sudden arousal from sleep, accompanied with screaming or crying out and intense fear, children often have no recollection of the dream content (AASM, 2005). Nightmares and bad dreams may contribute to the development of night-time fears where the child becomes afraid to fall asleep in fear of having a nightmare. Indeed, it has been estimated that around 80% of school-aged children experience night-time fears at some point (Gordon et al. 2007). While nightmares, bad dreams and night-time fears are common and considered normal, their occurrence may be related to other factors such as child temperament, media viewing, parental behaviour and psychological disorders (Moore 2012).

Enuresis: Enuresis (bed-wetting) typically occurs in around a third of children four years of age, and is only considered problematic when symptoms persist beyond 5 years of age (AASM, 2005). In adolescence, prevalence rates drop to around 1-2% (Nappo et al. 2002). Primary enuresis occurs when the child fails to arouse from sleep in response to the sensation of a full bladder, or through involuntary muscle contractions. Secondary enuresis, however, may be the result of a concomitant problem such as diabetes, urinary tract infections or neurologic pathologies amongst others (AASM, 2005). Hereditary factors are known to play a role, and some studies have identified chromosomal links on locations 22q, 13q and 12q (Arnell et al. 1997; Bakwin 1971; Eiberg 1998; von Gontard et al. 1998).

Sleep-related breathing disorders: Sleep disorders related to breathing difficulties are not uncommon in childhood. Sleep apnea is characterised by recurrent cessation of breathing during sleep, resulting in a reduction in blood oxygen saturation, sudden awakenings, sleep fragmentation, snoring and excessive daytime sleepiness (AASM, 2005). Such difficulties have severe adverse

consequences often leading to cognitive and behavioural difficulties and cardiovascular complications (AASM, 2005). Three types of sleep apnea can be distinguished: central, obstructive and mixed (consisting of symptoms of both central and obstructive sleep apnea). Central sleep apnea has an unknown aetiology and is characterised by the absence of ventilatory effort – that is, the individual fails to attempt to breathe throughout the night. Obstructive sleep apnea (OSA), on the other hand, is characterised by apnoeic events which occur as a result of obstruction of the upper airways during inspiration, often due to excess weight surrounding the neck and chest. While OSA largely occurs in middle-aged to older adults, both central and obstructive sleep apnea occur in children, and the prevalence of OSA in children is approximately 2%, most often in pre-schoolers (Ali et al. 1993; AASM, 2005). Primary sleep apnea of infancy consists of a multitude of possible symptoms common to all three sub-types, although central sleep apneas are most common (AASM, 2005). It is possible that its occurrence in infancy is a developmental disorder resulting from immature development of the brainstem and centres controlling respiration, and thus is more common in pre-term infants (AASM, 2005). Indeed prevalence rates range from 25% to 84% in pre-term infants weighing less than 2.5 kilograms and 1 kilogram, respectively (AASM, 2005). In such cases the disorder often disappears with maturity. OSA predominantly occurs in REM sleep, and unlike adults, the airway obstruction does not always lead to cortical arousal in children, and hence sleep architecture is less affected despite the presence of frequent hypoxia (AASM, 2005). As such, daytime sleepiness is less evident in children and adolescents as compared to adults (Halbower and Mahone 2006). The primary risk factors for OSA in childhood are larger than usual tonsils or adenoids, craniofacial abnormalities and neuromuscular diseases which lead the upper airways to collapse, and obesity (AASM, 2005). Indeed, since childhood obesity is on the rise, so too are complications such as OSA and sleep-disordered breathing (SDB) (Verhulst et al. 2008; Arens and Muzumdar 2010). SDB is defined as the partial or complete obstruction of the airways, leading to sleep fragmentation and ventilatory disruption. Unlike OSA, SDB is thought to reflect a continuum of difficulties including snoring, and is present in around 16% of children (Halbower and Mahone 2006). Both OSA and SDB have the potential to lead to long term neuropsychological impairments if left untreated, including depression, poor quality of life, low self-esteem, poor school performance, attention problems and hyperactivity (see Halbower and Mahone 2006, for a review). Twin studies in adults have demonstrated that genetic influences contribute to around 23-52% of variability in breathing related difficulties including daytime sleepiness related to OSA, SDB and snoring (Carmelli et al. 2001; Carmelli et al. 2004; Desai et al. 2004).

Narcolepsy: Narcolepsy is a disorder of abnormal sleep-wake cycling, characterised by frequent unintentional short naps or lapses into sleep, and periods of REM sleep soon after sleep

onset (after around 20 minutes from sleep onset, compared to the more typical 90 minutes), often coupled with cataplexy (a sudden, transient loss of muscle tone, often leading to collapse) (AASM, 2005). Excessive daytime sleepiness is often the first symptom to be detected. Other symptoms include extended nocturnal sleep, difficulty awakening after nocturnal sleep and aggressiveness upon awakening (Nevsimalova 2009). As well as sleep-related symptoms, narcolepsy also impacts on psychological functioning, including poor attention and concentration, depressed mood, and has been associated with interpersonal conflict (Nevsimalova 2009). Sleep attacks typically occur during monotonous activities but associated attacks of cataplexy can be triggered by intense emotion (AASM, 2005). Although narcolepsy is typically diagnosed in middle-adulthood, symptoms often first appear in childhood or adolescence (Nevsimalova 2009). Estimates of narcolepsy in the general population indicate that around 0.5% of adults experience the disorder (Dauvilliers et al. 2001; Ohayon et al. 2002; Silber et al. 2002); however prevalence rates in children are lacking (Nevsimalova 2009). Evidence of a familial pattern of narcolepsy is demonstrated by the fact that prevalence rates rise to 1-2% in first-degree relatives of those with narcolepsy (Nishino et al. 2000; Mignot 1998). Early twin studies report a possible hereditary component to narcolepsy (e.g. Imlah 1961). Studies investigating specific genes have identified sub-types of the human leukocyte antigen (HLA) gene (DR2/DRB1*1501, DQA1*0102, and DQB1*0602) as genetic markers for narcolepsy (see Chabas et al. 2003, for a review; Kadatoni et al. 2007). Although the HLA gene is clearly important, Pollmächer and colleagues highlight that while around 50% of first-degree relatives of narcoleptic patients also share the critical gene variant, few of these individuals develop the disorder, suggesting the importance of other genetic and/or environmental influences in its pathogenesis (Pollmächer et al. 1990). Indeed, the majority (around two thirds) of monozygotic twins are discordant for narcolepsy (see Mignot 1998, for a review), underscoring the importance of exogenous factors. Given the role of orexin/hypocretin in controlling the smooth transition from wake to sleep (Saper et al. 2010), it is also likely that genes controlling orexigenic mechanisms are important (Peyron et al. 2000). Indeed, the link between the hypocretin system and narcolepsy was first evidenced by the finding that canine narcolepsy was due to a mutation in the hypocretin receptor-2 gene (Lin et al. 1999). In humans, a single case study of infant-onset narcolepsy demonstrated a link between a mutation of the hypocretin gene (Nevsimalova et al. 2000).

Restless legs syndrome (RLS): RLS is characterised by unpleasant sensations in the legs, often involuntary leg twitches and periodic limb movements, and an irresistible urge to move the legs during rest (AASM, 2005). Symptoms worsen during the evening and are partially relieved by movement. Symptoms particularly occur during the transition from wake to sleep, resulting in difficulty initiating sleep as well as returning to sleep following an awakening. In some instances,

patients may be unaware of the sensations, putting their difficulty initiating sleep down to insomnia. Age of onset is typically in young adulthood, but symptoms are evident in some children. While around 5-10% of the adult population report symptoms consistent with a diagnosis of RLS, and around a quarter of these individuals report the onset of symptoms in childhood, few studies have estimated the prevalence in children and adolescents (Picchietti et al. 2007). RLS in children may be misdiagnosed simply as 'fidgetiness', normal growing pains, or ADHD given the similarity of the presenting symptoms (Maheswaran and Kushida 2006; Picchietti et al. 1999). One study reported definite RLS symptoms in around 1.9% of children aged 8-11 years, and 2% in teenagers aged 12-17 years (Picchietti et al. 2007). Iron deficiency is thought to precipitate the development of RLS. Indeed, lower than average serum ferratin levels (less than 50ng/mL) have been associated with increased symptom severity in adults with RLS (Sun et al. 1998), and individuals with conditions associated with iron deficiency are at greater risk (Rangarajan and D'Souza 2007). Pediatric studies have demonstrated similar findings with lower than average serum ferratin levels found in around 80% of children with RLS (Picchietti and Stevens 2007; Kotagal and Silber 2004). Furthermore, RLS is more common in females, and it is likely that this is particularly apparent during menstruation and pregnancy (Picchietti and Picchietti 2008). In addition to iron deficiency as a risk factor for RLS, RLS shows particularly high familial vulnerability. Indeed, diagnostic criteria for RLS in childhood (as compared to adult diagnosis) includes the additional criterion that a first-degree relative is also affected (AASM, 2005). In a population based pediatric study, around 71-80% of children with RLS had a positive parental history of the disorder (Picchietti et al. 2007). Heritability estimates of 54% and 60% for the symptoms of restless legs and leg jerking have been demonstrated in a sample of adult twins (Desai et al. 2004). Interestingly, other studies have demonstrated that early onset RLS (prior to 36 years of age) appears to be more severe and highly genetically influenced than late onset RLS (occurring after 36 years of age), which appears to occur in individuals with no familial history (De Cock Cochen and Dauvilliers 2010; Whittom et al. 2007). Studies attempting to determine a possible mode of transmission further reflect the genetic heterogeneity of early- versus late-onset subtypes. The involvement of a major gene, with autosomal-dominant mode of transmission is evident for early-onset RLS only; while late-onset RLS appears to be compatible with a model of free transmission (Winkelmann et al. 2002). In both cases, however, there is evidence for a role of a multifactorial component, with the possibility of other genetic and non-genetic factors (i.e. gender, environmental factors, iron status). Linkage studies have demonstrated a possible link to 5 chromosomal regions (including 12q, 14q13-21, 9q24-23, 2q33 and 20p13) (see Winkelmann et al. 2007, for a review). Gene association studies have demonstrated possible associations within genes coding dopaminergic transmission, and two mitochondrial genes coding monoamine oxidase

A and B (see Winkelmann et al. 2007, for a review). The link between RLS and dopaminergic transmission is perhaps not surprising given that pharmacological treatment with drugs that increase dopamine transmission alleviate symptoms (Winkelmann et al. 2007).

Sleep disturbances and associated traits

Sleep disturbances are associated with a plethora of difficulties in childhood and adolescence both concurrently and longitudinally (Gregory and Sadeh 2012). Indeed, all of the clinical syndromes discussed in this handbook have been associated with atypical sleep. Learning about these associations holds the promise to understand more about processes underlying both difficulties. Here we present examples of the known associations between sleep disturbances and ASDs, ADHD, schizophrenia, emotional (i.e. anxiety and depression) and behavioural difficulties.

Sleep and autism/ ASDs: Depending on sample composition and definition of sleep, sleep disturbances are prevalent in around 25-80% of children with ASDs (Richdale and Schreck 2009). Studies using subjective measures of sleep indicate that the most frequently reported symptoms include difficulty initiating sleep, frequent awakenings, short sleep time, restlessness during sleep and not falling asleep in own bed (Williams et al. 2004; Honomichl et al. 2002). Similarly, studies using objective measures of sleep, such as actigraphy, demonstrate longer sleep onset latencies, earlier morning awakening, increased night-waking and greater sleep fragmentation in children with autism compared to typically developing children (Wiggs and Stores 2004; Allik et al. 2008). Polysomnographic studies (PSG: a technique which measures electrical activity of the brain and body allowing us to determine sleep stages) have further demonstrated sleep abnormalities as indicated by decreased REM latency and shorter total sleep time (Miano et al. 2007; Elia et al. 2000). Severity of ASD also appears to be related to the severity of sleep disturbances (Mayes and Calhoun 2009). The evidence pointing to difficulties in the timing of sleep suggest that abnormalities of the circadian system may underlie such difficulties in autism. This theory is supported by evidence that children with autism exhibit abnormal cortisol and melatonin profiles (see Glickman 2010, for a review). The role of melatonin as a mechanism through which sleep disturbances manifest in children with ASD is also exemplified by the finding that such sleep disturbances are attenuated by pharmacological administration of melatonin (Paavonen et al. 2003). However, it is also likely that such sleep disturbances are influenced and exacerbated by behavioural difficulties in children with ASD, such as those consistent with limit-setting disorder and sleep-association disorder as outlined above.

Sleep and ADHD: Sleep disturbances are prevalent in around 25-50% of children with ADHD (Corkum et al. 1998), and a wealth of data exists on the links between these difficulties. One meta-analysis concluded that children with ADHD, in comparison to control children, exhibit greater subjectively reported bedtime resistance, sleep initiation difficulties, night-wakings, awakening early

in the morning, SDB and daytime sleepiness (Cortese et al. 2009a). Studies using actigraphy have also shown greater sleep-schedule variability in children with ADHD compared to controls (Gruber and Sadeh 2004). Genetic association studies have implicated a functional polymorphism in the catechol-O-methyltransferase (COMT) gene in the link between actigraphically assessed sleep disturbances and ADHD (Gruber et al. 2006). Findings using PSG are inconsistent, with one meta-analysis identifying no differences in sleep architecture between children with ADHD and controls (Sadeh et al. 2006). Contrastingly, another found significant differences to the extent that children with ADHD exhibited lower sleep efficiencies, more sleep stage shifts and an increased apnea-hypopnea index (Cortese et al. 2009a). The only consistent finding across studies is that children with ADHD appear to report more periodic limb movements (PLMs) than control children. Indeed, around 40% of children with ADHD (in the age range of 2-14 years) exhibit symptoms consistent with a diagnosis of RLS (Cortese et al. 2005). Iron deficiency is thought to be a common pathophysiological mechanism underlying this association (Konofal et al. 2007), and indeed a subset of children with ADHD and low serum ferratin levels have been shown to exhibit greater movements during sleep (Cortese et al. 2009b). Iron is necessary for the synthesis of dopamine (Earley et al. 2000), and while the complex relationship between RLS, PLMS, and ADHD is not yet fully understood, it is possible that these disorders share a common dopaminergic deficit (Walters et al. 2000). Indeed all three disorders respond to dopaminergic treatments (Maheswaran and Kushida 2006), strengthening the hypothesis that the dopamine pathway is important in explaining the links between these symptoms.

Furthermore, breathing difficulties such as SDB are commonly associated with inattention and hyperactivity characteristic of ADHD (Chervin et al. 2002). In one study, children with SDB exhibited more daytime sleepiness and hyperactivity than controls (Melendres et al. 2004). Evidence for a potential causal link between SDB and ADHD comes from the finding that pharmacological/ surgical treatment of SDB and sleep apnea often improves symptoms of inattention and hyperactivity (Chervin et al. 2002; Huang et al. 2007). Additionally, it is possible that deficits in the pre-frontal cortex as a result of oxygen desaturation results in disrupted attentional processing, exacerbating ADHD. Given that sleep deprivation and disruption are known to impact on neurobehavioural functioning in typically developing children (O'Brien 2009), it is likely that sleep disturbances of any type may exacerbate symptoms of inattentiveness, mood disturbances and paradoxical hyperactivity, and thus contribute to the aetiology of ADHD (Cortese et al. 2005).

Sleep and Schizophrenia: While childhood onset schizophrenia is rare, prevalence rates increase during adolescence to around 1% of the population by adulthood (Banaschewski 2008). Sleep disturbances, comparable to insomnia, occur in up to 80% of individuals with schizophrenia

and this is reported as one of the most frequent symptoms of this disorder (Wulff et al. 2012). As well as subjectively reported poor sleep quality, individuals with schizophrenia show abnormal architectural properties of sleep, including increased sleep latency, reduced REM latency, REM density, sleep efficiency, total sleep time and duration of SWS (Cohrs 2008). Additionally, individuals with schizophrenia often exhibit severe circadian disruption, including phase delays and advances, free-running rhythms, and irregular sleep-wake scheduling (Wulff et al. 2010). Improving sleep disturbances has been shown to improve negative symptoms associated with schizophrenia (Wulff et al. 2010). Evidence for a biologically mediated pathway between schizophrenia and sleep/circadian regulation has been demonstrated by genome-wide association studies (GWAS) which have shown links between schizophrenia and several genes known to govern sleep/ circadian regulation (see Wulff et al. 2010, for a review).

Sleep and emotional difficulties: Links between sleep and emotional difficulties such as anxiety and depression in adulthood are well established. However, understanding these associations in childhood has only relatively recently come to the fore, and have conceptualised sleep disturbances and emotional difficulties in a number of ways. Studies combining anxiety/depression have demonstrated that trouble sleeping was associated with parent reported anxiety/depression when the children were aged 6 and also at age 11 (Johnson et al. 2000). Another study reported associations between anxiety/depression and a composite measure of sleep disturbance in children between the ages of 4 and 15 years (Gregory and O'Connor 2002). Interestingly, studies comparing these associations in different age groups have shown that associations appear greater in middle childhood and adolescence as compared to early childhood (Gregory and O'Connor 2002; Johnson et al. 2000). It is possible that sleep disturbances in young children are part of normal development and so less problematic compared to their occurrence in later childhood/adolescence when they may be more indicative of a problem.

When examining anxiety exclusively, studies have shown that the sleep-related problems are prevalent in around 88% of youths with anxiety disorders (Alfano et al. 2007). As well as studies examining subjective reports of poor sleep, findings of sleep disturbance in children with anxiety is also corroborated by studies assessing sleep using PSG as indexed by increased night-wakings and longer sleep onset latency compared to controls and those with depression (Forbes et al. 2008). One study specifically focusing on generalised anxiety disorder (GAD) found increased sleep onset and REM sleep latencies in 7-11 year old children with GAD compared to controls (Alfano et al. 2012). Other studies have distinguished anxiety subtypes and associated sleep disturbances. For example, in one study sleep difficulties in childhood were associated with all types of anxiety examined; however, during adolescence, sleep disturbance appeared to be associated with certain types of

anxiety (generalized anxiety, panic/agoraphobia and social anxiety) more than others (obsessive compulsive symptoms and separation anxiety) (Alfano et al. 2009).

Studies examining depression exclusively have also found associations with sleep disturbances in children and adolescents (for a review see Ivanenko et al. 2005). As with mixed anxiety/depression and anxiety, these associations appear to be influenced by age, with associations between sleep disturbances and depression being stronger in adolescents compared to children (Alfano et al. 2009). Furthermore, in another study, hypersomnia was reported less frequently in children with Major Depressive Disorder (MDD) than adolescents with MDD (Ryan et al. 1987). Indeed sleep complaints are high in adolescents with MDD with around 88% of adolescents with MDD experiencing some type of sleep complaint, typically nonrestorative sleep or insomnia (Urrila et al. 2012). Using PSG to measure sleep, studies have shown that children with depression experienced shorter REM sleep latency (time in minutes from sleep onset to first REM sleep episode), longer sleep latency and REM sleep duration and a higher number of night-wakings compared to controls (Arana-Lechuga et al. 2008). Short REM sleep latency (~ 60 minutes) has often been considered to be a biological marker of depression in adults (Kupfer 1976), and has been reported in other samples of children and adolescents suffering depression (Emslie et al. 1990; Lahmeyer et al. 1983). However, other studies have failed to find polysomnographically defined sleep changes in children and adolescents with depression compared to controls (see Gregory and Sadeh 2012, for a review). Taken together, current research suggests that subjective sleep complaints in depression are more common than those identified using objective measures. The discrepancy between subjective and objective measures of sleep is consistent with polysomnographic studies of insomnia. While individuals with insomnia typically report difficulty initiating sleep and frequent night-wakings, objective data do not support these claims (Riemann et al. 2010). Thus, as in insomnia, it is possible that the sleep complaints in depression are almost exclusively subjective and may be the consequence of sleep-state misperception during and following sleep.

In addition to examining concurrent associations between sleep disturbances and emotional difficulties, numerous studies have also examined these associations longitudinally. The majority of studies within this area demonstrate that sleep disturbances in childhood or adolescence predict later anxiety (Gregory et al. 2005a) and depression (Roane and Taylor 2008; Roberts et al. 2002), although not all studies are consistent (Johnson et al. 2000; Gregory et al. 2005a). One study which demonstrated that sleep disturbances predicted later depressive symptoms at one year follow-up in a sample of adolescents, and that this association was partially mediated by catastrophic worry (Danielsson et al. 2012). Few studies have examined the opposite direction of effects: that emotional

difficulties predict subsequent sleep disturbances. However, while associations are likely to be bidirectional, there is less support for the possibility that depressive symptoms forecast later sleep problems (Gregory and O'Connor 2002; Gregory et al. 2009c). One study which examined the order of effects of insomnia, anxiety and depression using retrospective reports in adolescents demonstrated that anxiety disorders preceded insomnia in 73% of comorbid cases whereas insomnia preceded depression in 69% of comorbid cases (Johnson et al. 2006). It thus appears that insomnia may be associated with anxiety and depression differentially. One explanation for this conclusion focuses on hyperarousal, which has been implicated in anxiety but not depression (Clark and Watson 1991). The role for hyperarousal in some cases of insomnia is well established (Riemann et al. 2010), and it is possible that hyperarousal may be a vulnerability factor for anxiety and insomnia.

Identifying the mechanisms underlying the associations between sleep and emotional difficulties has been a focus of much research. Twin studies have shed much light on the possible factors involved in the associations between sleep and related difficulties. One twin study demonstrated that parent reports of sleep disturbances in 3 year old twins were genetically unrelated to other traits assessed, including oppositionality; withdrawn/depressed behaviour; aggressive behaviour; anxious behaviour and overactivity (Van den Oord et al. 2000). Shared environmental factors (those that make individuals within a family similar) appeared to influence the whole range of difficulties. Contrastingly, a study focusing on 8 year old twins demonstrated that the link between sleep disturbance and depression was largely influenced by genes (Gregory et al. 2006), as was the longitudinal association between sleep at 8 years of age and depression symptoms at 10 years (Gregory et al. 2009c). Molecular genetic studies have shed light on specific genetic variants influencing the associations between sleep and emotional difficulties. For example, genes involved in the serotonin pathways are likely to play a role in the associations between sleep and anxiety given the role of serotonin with regards to each phenotype (Jouvet 1969; Lesch et al. 1996). As well as identifying genetic influences, specifying environmental influences common to both phenotypes is also informative. Indeed, both family disorganization and maternal depression have been shown to correlate moderately with both sleep disturbance and anxiety symptoms in 3-4 year old children and accounted for some of the association between the two difficulties (Gregory et al. 2005b). Other candidate environmental influences include being a bully victim, which is associated with poor sleep and feeling sad (Williams et al. 1996) and socioeconomic status which is associated with poor sleep and a whole host of other difficulties (Buckhalt et al. 2007; Miech et al. 1999; Bøe et al. 2012). The role of parenting in sleep development and sleep disturbances has been repeatedly demonstrated, particularly in early childhood (Sadeh et al. 2010). As with sleep disturbances, different aspects of parenting are also known to be associated with emotional and behavioural difficulties (e.g. Gregory

and O'Connor 2002). Thus, it is conceivable that parenting explains some of the shared variability between sleep and emotional problems.

As well as specifying genetic and environmental influences to provide clues as to the mechanisms underlying these associations, it is also worthwhile to consider candidate hormonal and neural pathways through which these influences may take effect. One hormone which is likely to play a role in the association between sleep and emotional difficulties is cortisol. Cortisol is a hormone which is released in response to stress, but also exhibits a stable diurnal rhythm and has been linked to sleep (Elder et al. in press). The HPA axis, which controls reactivity to stress, is likely to be involved in the associations between sleep and emotional difficulties. Imaging studies have found brain abnormalities during wakefulness and sleep, such as hypofrontality, and sleep related decrements in fronto-parietal areas in individuals with depression (Armitage 1995; Germain et al. 2004). The link between sleep and depression is also demonstrated by the finding that acute sleep deprivation, which challenges sleep homeostasis, temporarily ameliorates depressive symptoms (Giedke and Schwarzler 2002).

Sleep and Behavioural Difficulties: Associations between sleep disturbances and behavioural problems such as aggression and conduct disorder have received less attention, although there are indications that these disorders are also linked. Many studies, based on subjective or parental reports, find associations between sleep disturbances, insufficient sleep and behavioural problems. For example, sleep-disordered breathing, RLS and PLMS have been associated with conduct problems (Chervin et al. 2003). Other sleep issues such as sleeping less than others have also been associated with behavioural difficulties (Goodnight et al. 2007; Gregory et al. 2008a). Studies using actigraphy and teachers' or parental ratings of behaviour problems have also reported significant correlations between short sleep time or poor sleep quality and behavioural difficulties in school-age children (Aronen et al. 2000; Sadeh et al. 2002), although a similar study in adolescents failed to find such relationships (Moore et al. 2009), possibly highlighting the importance of age when considering these phenotypic associations.

As previously mentioned, twin studies have demonstrated possible overlap in the shared environmental influences affecting both sleep and behavioural difficulties. In addition, shared genes are likely to be involved. For example, a variant of the MAO-A gene, which has previously been associated with sleep and aggression (Alia-Klein et al. 2008; Brummett et al. 2007), is a good candidate to further explore with regards to the links between these and related phenotypes.

Conclusion and Future Directions

The importance of sleep over the life course, especially during developmental periods sensitive to brain maturation and behavioural/emotional growth such as childhood and adolescence,

is unequivocal. The combination of different techniques, including large-scale population based longitudinal studies, quantitative genetics, gene association studies, GWAS, and brain imaging has allowed sleep researchers to answer many questions related to the understanding of normal sleep processes, as well as the aetiology and symptomology of a multitude of disorders of sleep and wakefulness. Knowledge of these underlying mechanisms has the potential to advance the developments of novel treatments for sleep disorders.

Furthermore, while research has come a long way to acknowledging the abnormalities that can occur in sleep, as well as those that co-occur with numerous other disorders, much work is still required to further our understanding of the mechanisms underlying normal sleep, sleep disturbances, and associations with other disorders. It is likely that a multitude of interacting neurobiological, genetic and environmental factors are at play, as well complex epigenetic processes. Knowledge of the changes in normal sleep across the lifespan, developmental sensitivities to sleep disturbances, and longitudinal associations between difficulties suggests that identifying and treating sleep disturbances early in childhood and adolescence has the potential to halt the development of further difficulties, enabling the development of a healthy, soundly sleeping generation.

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	Stage 1	Stage 2	Stage 3 & 4 (SWS)	REM	Total sleep (hours)
Newborn	~20-50%	Start to emerge		~50-80%	~17-19
3-6 months	~25-49%			~34-55%	~14
1 year	~51-61%			~26-40%	~13
2 years	~75%			~25%	~12

Table 1. Proportion of night spent in sleep stages from infancy to 2-years. Estimates accumulated from Carskadon & Dement (2011); Crabtree & Williams (2009); and Roffwarg, Muzio & Dement (1966).

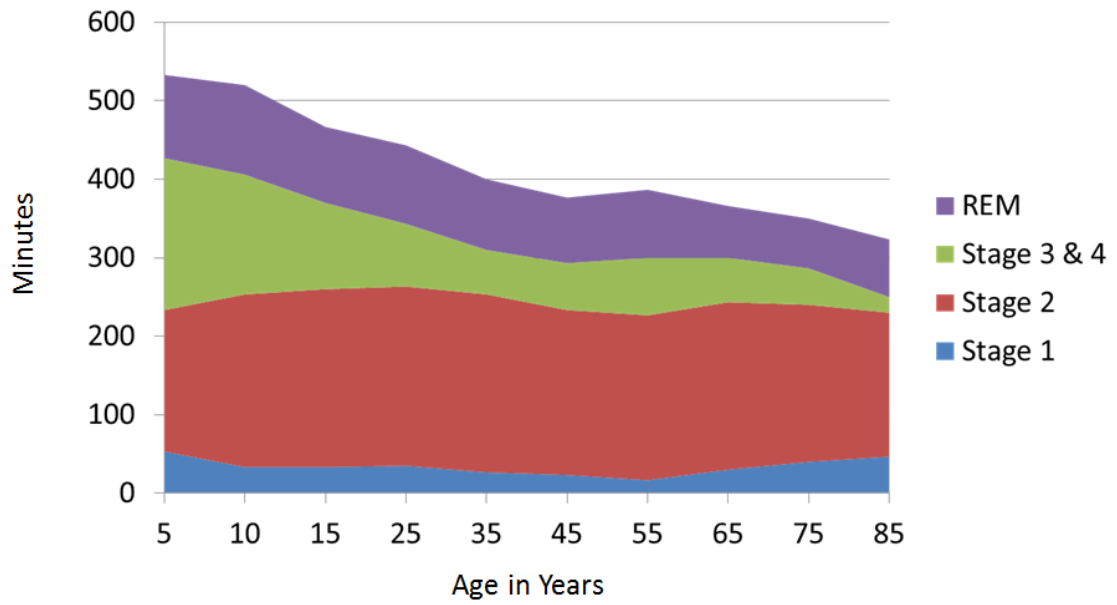

Figure 1. Minutes of the night spent in sleep stages across the lifespan. Data from Ohayon et al (2004).